REMARKS/ARGUMENTS

Summary of Examiner Interview

Applicants thank Examiner Weddington for the courtesies extended to the undersigned attorney and Robert W. Esmond during the personal interview conducted on January 25, 2006. During the course of the Examiner interview, the claim amendments and remarks/arguments as substantially set forth herein were discussed. The Examiner acknowledged the reasonableness of Applicants' position and indicated that he would further consider the matter upon receipt of this written reply to the Office Action.

Information Disclosure Statement

An Information Disclosure Statement, identifying References CD-CI, is submitted herewith. Applicants also request the Examiner to initial and return to Applicants a copy of the PTO-1449 form that accompanied the Information Disclosure Statement dated December 8, 2004, so as to confirm the Examiner's consideration of Reference CB.

The Pending Claims

Claims 1-4, 6-20, and 22-37 are currently pending. Reconsideration of the pending claims, as amended, is hereby requested in view of these remarks/arguments.

Discussion of Claim Amendments Relative to Issued Claims

Claim 1 has been amended to remove the recitation of gossypol and a physiologically acceptable salt thereof. As a result, claim 5 has been canceled as superfluous, and claims 6 and 7 have amended to be dependent on claim 4 rather than claim 5.

Claim 8 has been amended to replace the term "compound" with the term "composition" and to replace the term "gossypol" with the term "(-)-gossypol." In addition, claim 8 has been amended to recite the phrase "wherein said composition rotates the plane of polarized light in the (-) direction" for additional clarity. These claim amendments are supported by the specification at, for example, column 7, lines 29-66. Claims 11-14 have been amended to ensure proper antecedent basis for the claim terms therein in view of the amendment of claim 8. In addition, claim 11 has been amended to recite a blood level of "200-1000 ng/dl" as supported by the specification at, for example, column 7, Table 4.

Claims 15-20 and 22-37 are new claims, which are supported by the specification at, for example, column 2, lines 20-25, and column 7, lines 29-34. Specifically, claims 15 and 16, depending from claims 1 and 8, respectively, further recite that the cancer is a carcinoid tumor of neuroendocrine tissue located in the lung, pancreas, or gastrointestinal tract. Independent claims 17 and 24 are similar to issued claims 2 and 9, respectively, except that claims 17 and 24 also recite that the cancer can be a carcinoid tumor of neuroendocrine tissue located in the lung, pancreas, or gastrointestinal tract. Dependent claims 18-23 and 25-30 are similar to original claims 2-7 and 9-14, respectively. Claims 31-37 are directly or indirectly dependent on claim 24 and either recite that the gossypol is (-)-gossypol or more specifically define the cancer.

The amended claims and the newly added claims, therefore, narrow the scope of the issued claims, and no new matter has been added by way of these amendments.

Discussion of Claim Amendments Relative to Immediately Previous Claim Set

The claim set presented herein includes additional amendments to the amended claim set presented in Applicants' reply to the Office Action dated December 21, 2004.

In particular, claim 1 has been further amended to remove the recitation of (-)-gossypol and a physiologically acceptable salt of (-)-gossypol, which previously replaced the recitation of gossypol and a physiologically acceptable salt of gossypol. Claim 4 has been amended to place it back in its issued form by reciting a blood concentration of "400-1000 ng/dl" in place of "200-1000 ng/dl." Claim 5 has now been canceled as superfluous in view of the amendment of claim 1.

Claim 8 has been further amended to (a) replace the term "compound" with the term "composition" and (b) recite "wherein the composition rotates the plane of polarized light in the (-) direction." Claim 8 previously had been amended to (a) replace the term "gossypol" with the term "(-)-gossypol" and (b) replace the term "pharmaceutically" with the term "physiologically." The amendments to claims 11-14 described above relative to the issued claims constitute additional amendments to these claims, with the exception of the recitation in claim 11 of a blood concentration of "400-1000 ng/dl" in place of "200-1000 ng/dl" (which change was previously made to claim 11).

Claims 15-30 were previously presented, but additional amendments have been made to these claims. Specifically, claim 17 has been further amended to remove the recitation of

gossypol and a physiologically acceptable salt of gossypol. Claim 19 has been amended to change its dependency from claim 18 to claim 17. Claim 21 has been canceled, and the dependencies of claims 22 and 23 have been changed from claim 21 to claim 20. The dependency of claim 26 has been changed from claim 25 to claim 24.

Claims 31-37 are newly presented relative to the previous set of amended claims.

The Office Action

Claims 1 and 8 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Yerukhimov et al. (*Voprosy Onkologii*, 12(2): 29-34 (1966)).

Claims 2, 8 [*sic* – 18], 9, 17, 24, and 25 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Yerukhimov et al. in view of Band et al. (*Gynecologic Onc.*, 23(2): 261 (1986)) and Band et al. (*Gynecologic Onc.*, 32: 273-277 (1989)).

Claims 3-7, 10-16, 19-23, and 26-30 have been indicated as allowable.

Discussion of Rejection Under 35 U.S.C. § 102(b)

The Office contends that Yerukhimov et al. teaches the use of a racemic gossypol composition (i.e., a mixture of the (+) and (-) enantiomers of gossypol) to treat bladder tumors, thereby anticipating the subject matter of claims 1 and 8.

Yerukhimov et al. refers to Vermel et al. (*Voprosy Onkologii*, 9(12): 39-41 (1963)) as regards the isolation and structure of the gossypol used in studies reported therein. *See* English translation of Yerukhimov et al. at page 31. Vermel et al. discloses the isolation of gossypol from the cotton plant *Gossypium hirsutum*. *See* Vermel et al. at page T106, paragraph 6. Furthermore, Zhou et al. (*Contraception*, 37(3): 239-245 (1988)) states that gossypol derived from *Gossypium hirsutum* is "always dextrorotatory caused by an excess of (+)-gossypol." *See* Abstract of Zhou et al. In addition, Cass et al. (*J. Agric. Food Chem.*, 52: 5822-5827 (2004)) reports on the enantiomeric ratios of gossypol derived from different samples of *Gossypium hirsutum*. See Table 1 on page 5823 of Cass et al. All of these additional references (copies of which are provided by way of the concurrently filed Information Disclosure Statement) confirm that the racemic gossypol composition disclosed in Yerukhimov et al. was a (+)-gossypol composition (i.e., a composition with an excess of (+)-gossypol), rather than a (-)-gossypol composition (i.e., a composition with an excess of (-)-gossypol).

Claim 1, as amended, does not recite gossypol or a physiologically acceptable salt thereof, but rather merely recites gossypolone and a physiologically acceptable salt thereof. Inasmuch as Yerukhimov et al. does not disclose a method of treating cancer involving the use of gossypolone or a physiologically acceptable salt thereof, the anticipation rejection of claim 1 is inappropriate and should be withdrawn.

Claim 8, as amended, recites the use of a (-)-gossypol *composition*, rather than the use of a (-)-gossypol *compound*. As discussed above, Yerukhimov et al. does not disclose the use of a (-)-gossypol composition. Accordingly, Yerukhimov et al. does not anticipate the subject matter of claim 8. The anticipation rejection of claim 8 is not appropriate and should be withdrawn.

Discussion of Rejection Under 35 U.S.C. § 103

The Office contends that the subject matter of claims 2, 8 [*sic* – 18], 9, 17, 24, and 25 would have been obvious to one of ordinary skill in the art at the relevant time in view of the combined disclosures of Yerukhimov et al., Band et al. (1986), and Band et al. (1989).

As discussed above, Yerukhimov et al. discloses the use of a (+)-gossypol composition to treat bladder tumors. Band et al. (1986) discloses the *in vitro* testing of gossypol optical isomers on cell lines of ovarian, testicular, and gestational origin. Further, Band et al. (1986) discloses that (-)-gossypol is more potent than (+)-gossypol and may be clinically useful in the treatment of reproductive tract cancers. Finally, Band et al. (1989) restates the potency of (-)-gossypol relative to (+)-gossypol, and proceeds to state that the anti-proliferative action of gossypol is non-selective, thereby making it lethal to normal, non-cancerous, reproductive tract cells.

Claims 2 and 18, as amended, as well as claims 1 and 17 from which claims 2 and 18 are dependent, do not recite gossypol or a physiologically acceptable salt thereof, but rather recite the use of gossypolone or a physiologically acceptable salt thereof in the treatment of a cancer in a human. Yerukhimov et al. does not disclose a method of treating any cancer involving the use of gossypolone or a physiologically acceptable salt thereof, and Band et al. (1986) and Band et al. (1989) do not disclose the *in vivo* use of gossypolone or a physiologically acceptable salt thereof in the treatment of cancer. Moreover, none of these cited references would have provided one of ordinary skill in the art with a reasonable expectation of success as regards the use of gossypolone or a physiologically acceptable salt

thereof in the treatment of a cancer in a human. Accordingly, the subject matter of claims 2 and 18, as well as that of claims 1 and 17, would not have been obvious in view of the cited references.

Claim 9, as amended, as well as claim 8 from which claim 9 is dependent, recites the use of a (-)-gossypol composition or a (-)-gossypol physiologically acceptable salt composition to treat a cancer in a human. Yerukhimov et al. does not disclose a method of treating any cancer involving the use of a (-)-gossypol composition or a (-)-gossypol physiologically acceptable salt composition, rather Yerukhimov et al. discloses the use of a (+)-gossypol composition. Moreover, while Band et al. (1986) and Band et al. (1989) disclose the increased potency of (-)-gossypol relative to (+)-gossypol in the context of *in vitro* inhibitory effects on reproductive cancer cell lines, Band et al. (1989) proceeds to describe the non-selective inhibitory action of (-)-gossypol, which is detrimental to the functioning of normal, non-cancerous cells *in vivo*. Thus, aside from the fact that the cited references do not establish a correlation between *in vitro* testing of (-)-gossypol on cell lines and *in vivo* efficacy of treating a cancer in a human with (-)-gossypol, Band et al. (1989) teaches away from the invention by indicating that the use of (-)-gossypol can be harmful. Under the circumstances, a person having ordinary skill in the art at the relevant time would not have had a reasonable expectation of success in using a (-)-gossypol composition or a (-)-gossypol physiologically acceptable salt composition to treat any cancer in a human. Accordingly, the subject matter of claim 9, as well as that of claim 8, would not have been obvious in view of the cited references.

Claims 24 and 25 recite the use of gossypol or a physiologically acceptable salt thereof to treat certain specified cancers in a human. Yerukhimov et al. does not disclose a method of treating such cancers, but rather discloses the treatment of bladder tumors. Moreover, Band et al. (1986) and Band et al. (1989) merely disclose the *in vitro* inhibitory effects of gossypol on cancer cell lines. The cited references, however, do not establish a correlation between *in vitro* testing of gossypol on cell lines and *in vivo* efficacy of treating a cancer in a human with gossypol. Under the circumstances, a person having ordinary skill in the art at the relevant time would not have had a reasonable expectation of success in using gossypol or a physiologically acceptable salt of gossypol to treat any of the specified cancers of claims 24 and 25 in a human. Accordingly, the subject matter of claims 24 and 25 would not have been obvious in view of the cited references. Applicants additionally note that new

claims 31-37 are directly or indirectly dependent on claim 24 and recite that (a) the gossypol is (-)-gossypol and/or (b) the cancer is thyroid, pituitary, prostate, or breast cancer, or the cancer is a carcinoid tumor of neuroendocrine tissue located in the lung, pancreas, or gastrointestinal tract, thereby being even further removed from the disclosures of the cited references.

Accordingly, the cancer treatment methods defined by claims 2, 9, 17, 18, 24, and 25, as well as new claims 31-37, would not have been obvious to one of ordinary skill in the art in view of the cited references. The obviousness rejection is not appropriate and should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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